PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07K 14/775 | A3

(11) International Publication Number: WO 99/50286

(43) International Publication Date: 7 October 1999 (07.10.99)

(21) International Application Number: PCT/US99/06580

(22) International Filing Date: 25 March 1999 (25.03.99)

(30) Priority Data:
60/080,131 31 March 1998 (31.03.98) US

(71) Applicant *(for all designated States except US)*: UNIVERSITY OF CINCINNATI [US/US]; Room G–7 – Wherry Hall, Mail Location 0829, Cincinnati, OH 45267 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: HUI, David, Y. [US/US]; 3460 Sherbrooke Drive, Cincinnati, OH 45241 (US). TSO, Patrick [US/US]; 220 Carrington Place #310, Loveland, OH 45140 (US).

(74) Agents: OBERHAUS, Geoffrey, L. et al.; Dinsmore & Shohl LLP, 1900 Chemed Center, 255 East Fifth Street, Cincinnati, OH 45202 (US).

(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
18 November 1999 (18.11.99)

(54) Title: ANTIOXIDANT PEPTIDES DERIVED FROM APOLIPOPROTEIN A-IV

(57) Abstract

The present invention provides a method and means for inhibiting lipid oxidation. In accordance with the present invention, a number of novel lipid oxidation suppressant peptides, derived from apolipoprotein A–IV, have been made. These peptides possess lipid oxidation inhibiting properties which when administered orally or intravenously, can be used to decrease atherosclerosis. Since the peptides comprise specific portions of the native apo A–IV protein, there should be no immunogenicity problems associated with their administration to humans.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
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BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

INTERNATIONAL SEARCH REPORT

[redacted]ional Application No
PCT/US 99/06580

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07K14/775

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 2 686 605 A (RHONE-POULENC RORER S.A.) 30 July 1993 (1993-07-30) claims 1,15-17 ---	1,2
A	WO 95 25749 A (RESEARCH CORPORATION TECHNOLOGIES INC.) 28 September 1995 (1995-09-28) seq. id. nos.1,2,6 and 7 abstract --- -/--	1-4, 14-27, 31, 35-38, 45,52

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 September 1999	28/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Alvarez Alvarez, C

1

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/06580

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DUVERGER ET AL.: "Protection against atherogenesis in mice mediated by human apolipoprotein A-IV" SCIENCE, vol. 273, 16 August 1996 (1996-08-16), pages 966--968, XP002115081 cited in the application page 968; figure 1 ---	1,14
A	CAREW ET AL.: "Antiatherogenic effect of probucol..." PROC. NAT. ACAD. SCI. USA, vol. 84, November 1987 (1987-11), pages 7725-7729, XP000651844 cited in the application Discussion ---	1,14
A	COHEN ET AL.: "Reduced aortic lesions and elevated high density lipoprotein levels..." THE JOURNAL OF CLINICAL INVESTIGATION, vol. 99, no. 8, April 1997 (1997-04), pages 1906-1916, XP002115082 cited in the application Discussion ---	1,14
X,P	QIN ET AL.: "Apolipoprotein AIV: a potent endogenous inhibitor of lipid oxidation" AMERICAN JOURNAL OF PHYSIOLOGY, vol. 43, no. 5, May 1998 (1998-05), pages H1836-H1840, XP002115083 the whole document -----	1,2,14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/ 06580

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 1-34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/06580

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR 2686605 A	30-07-1993	CA 2125877 A	05-08-1993
		EP 0624194 A	17-11-1994
		WO 9315198 A	05-08-1993
		JP 7503367 T	13-04-1995
WO 9525749 A	28-09-1995	EP 0751961 A	08-01-1997
		JP 9510715 T	28-10-1997
		US 5840688 A	24-11-1998

PCT

RLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07K 14/00 | A2

(11) International Publication Number: WO 99/50286

(43) International Publication Date: 7 October 1999 (07.10.99)

(21) International Application Number: PCT/US99/06580

(22) International Filing Date: 25 March 1999 (25.03.99)

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60/080,131 31 March 1998 (31.03.98) US

(71) Applicant *(for all designated States except US)*: UNIVERSITY OF CINCINNATI [US/US]; Room G–7 – Wherry Hall, Mail Location 0829, Cincinnati, OH 45267 (US).

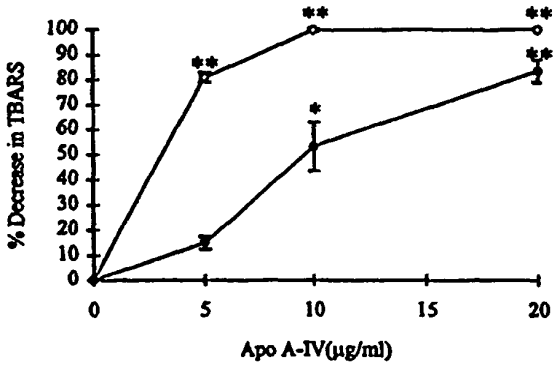
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: HUI, David, Y. [US/US]; 3460 Sherbrooke Drive, Cincinnati, OH 45241 (US). TSO, Patrick [US/US]; 220 Carrington Place #310, Loveland, OH 45140 (US).

(74) Agents: OBERHAUS, Geoffrey, L. et al.; Dinsmore & Shohl LLP, 1900 Chemed Center, 255 East Fifth Street, Cincinnati, OH 45202 (US).

(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
Without international search report and to be republished upon receipt of that report.

(54) Title: ANTIOXIDANT PEPTIDES



(57) Abstract

The present invention provides a method and means for inhibiting lipid oxidation. In accordance with the present invention, a number of novel lipid oxidation suppressant peptides, derived from apolipoprotein A–IV, have been made. These peptides possess lipid oxidation inhibiting properties which when administered orally or intravenously, can be used to decrease atherosclerosis. Since the peptides comprise specific portions of the native apo A–IV protein, there should be no immunogenicity problems associated with their administration to humans.

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IDS

WO 99/50286
PCT/US99/06580

ATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:
OBERHAUS, Geoffrey, L.
Dinsmore & Shohl LLP
1900 Chemed Center
255 East Fifth Street
Cincinnati, OH 45202
ÉTATS-UNIS D'AMÉRIQUE

Date of mailing (day/month/year) 07 October 1999 (07.10.99)	
Applicant's or agent's file reference 10738-17 PCT	**IMPORTANT NOTICE**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/US99/06580	25 March 1999 (25.03.99)	31 March 1998 (31.03.98)

Applicant
UNIVERSITY OF CINCINNATI et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
 EP,JP,US

 In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
 None

 The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
 07 October 1999 (07.10.99) under No. WO 99/50286

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, **a demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer
J. Zahra

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
10738-17 PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 99/06580	25/03/1999	31/03/1998
Applicant		
UNIVERSITY OF CINCINNATI et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

 a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

 [] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

 b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

 [X] contained in the international application in written form.

 [] filed together with the international application in computer readable form.

 [] furnished subsequently to this Authority in written form.

 [X] furnished subsequently to this Authority in computer readble form.

 [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

 [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

 [] the text is approved as submitted by the applicant.

 [X] the text has been established by this Authority to read as follows:

 ANTIOXIDANT PEPTIDES DERIVED FROM APOLIPOPROTEIN A-IV

5. With regard to the **abstract,**

 [X] the text is approved as submitted by the applicant.

 [] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

 [] as suggested by the applicant.

 [X] because the applicant failed to suggest a figure.

 [] because this figure better characterizes the invention.

 [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/06580

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 1-34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/06580

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07K14/775

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	FR 2 686 605 A (RHONE-POULENC RORER S.A.) 30 July 1993 (1993-07-30) claims 1,15-17 ---	1,2
A	WO 95 25749 A (RESEARCH CORPORATION TECHNOLOGIES INC.) 28 September 1995 (1995-09-28) seq. id. nos.1,2,6 and 7 abstract --- -/--	1-4, 14-27, 31, 35-38, 45,52

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 September 1999	28/09/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Alvarez Alvarez, C

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/06580

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	DUVERGER ET AL.: "Protection against atherogenesis in mice mediated by human apolipoprotein A-IV" SCIENCE, vol. 273, 16 August 1996 (1996-08-16), pages 966--968, XP002115081 cited in the application page 968; figure 1 ---	1,14
A	CAREW ET AL.: "Antiatherogenic effect of probucol..." PROC. NAT. ACAD. SCI. USA, vol. 84, November 1987 (1987-11), pages 7725-7729, XP000651844 cited in the application Discussion ---	1,14
A	COHEN ET AL.: "Reduced aortic lesions and elevated high density lipoprotein levels..." THE JOURNAL OF CLINICAL INVESTIGATION, vol. 99, no. 8, April 1997 (1997-04), pages 1906-1916, XP002115082 cited in the application Discussion ---	1,14
X,P	QIN ET AL.: "Apolipoprotein AIV: a potent endogenous inhibitor of lipid oxidation" AMERICAN JOURNAL OF PHYSIOLOGY, vol. 43, no. 5, May 1998 (1998-05), pages H1836-H1840, XP002115083 the whole document -----	1,2,14

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/06580

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR 2686605 A	30-07-1993	CA 2125877 A	05-08-1993
		EP 0624194 A	17-11-1994
		WO 9315198 A	05-08-1993
		JP 7503367 T	13-04-1995
WO 9525749 A	28-09-1995	EP 0751961 A	08-01-1997
		JP 9510715 T	28-10-1997
		US 5840688 A	24-11-1998

TENT COOPERATION TRE Y

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 20 December 1999 (20.12.99)	
International application No. PCT/US99/06580	**Applicant's or agent's file reference** 10738-17 PCT
International filing date (day/month/year) 25 March 1999 (25.03.99)	**Priority date** (day/month/year) 31 March 1998 (31.03.98)
Applicant HUI, David, Y. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

18 October 1999 (18.10.99)

[] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Christelle Croci
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

3022105

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09623006

PATENT COOPERATION TREATY

PCT

REC'D 08 DEC 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 10738-17 PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/06580	International filing date *(day/month/year)* 25 MARCH 1999	Priority date *(day/month/year)* 31 MARCH 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant UNIVERSITY OF CINCINNATI		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 60 sheets.

 ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of 18 sheets.

3. This report contains indications relating to the following items:

 - I [X] Basis of the report
 - II [] Priority
 - III [] Non-establishment of report with regard to novelty, inventive step or industrial applicability
 - IV [X] Lack of unity of invention
 - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI [] Certain documents cited
 - VII [] Certain defects in the international application
 - VIII [] Certain observations on the international application

CORRECTED VERSION

Date of submission of the demand	Date of completion of this report
18 OCTOBER 1999	21 JUNE 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer DEVESH SRIVASTAVA, PH.D.
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/06580

I. Basis of the report

1. With regard to the elements of the international application:*

[] the international application as originally filed

[X] the description:
pages (See Attached), as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

[X] the claims:
pages (See Attached), as originally filed
pages _____, as amended (together with any statement) under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

[X] the drawings:
pages (See Attached), as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

[X] the sequence listing part of the description:
pages (See Attached), as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[] the language of publication of the international application (under Rule 48.3(b)).

[] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[X] contained in the international application in printed form.

[X] filed together with the international application in computer readable form.

[] furnished subsequently to this Authority in written form.

[] furnished subsequently to this Authority in computer readable form.

[] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. 62

[X] the drawings, sheets/~~fig~~ NONE

5. [] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/06580

IV. Lack of unity f inv ntion

1. In response to the invitation to restrict or pay additional fees the applicant has:

 [X] restricted the claims.

 [] paid additional fees.

 [] paid additional fees under protest.

 [] neither restricted nor paid additional fees.

2. [] This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

 [] complied with.

 [X] not complied with for the following reasons:

Please See Supplemental Sheet.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

 [] all parts.

 [X] the parts relating to claims Nos. 1-25.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/06580

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-25	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-25	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-25	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-25 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method of treating [medical] conditions associated with lipid oxidation, specifically those conditions associated with atherosclerosis, by use of apolipoprotein A-IV compounds defined by SEQ ID NO:1-13.

---------- NEW CITATIONS ----------

NONE

Supplem ntal Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): A61K 38/00; C07K 14/775 and US Cl.: 514/12, 13, 14, 15, 16; 530/324, 326, 327, 328, 329, 359

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-7 9-10 12-44, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
Page 8, and 11, filed with the letter of 10 May 2000.

This report has been drawn on the basis of the claims,
page(s) NONE, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
pages 52-67, filed with letter of 10 MAY 2000.

This report has been drawn on the basis of the drawings,
page(s) 1-4, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) 44-51, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

IV. LACK OF UNITY OF INVENTION:

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2, and 13.3 is not complied with for the following reasons:
As applicant was previously notified this International Preliminary Examining Authority has found plural inventions claimed in the International Application covered by the claims indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-27, drawn to a method of treating conditions associated with lipid oxidation.
Group II, claims 28-34, drawn to a method of preventing oxidation in a lipid-containing food.
Group III, claims 35-41, drawn to a method of preventing oxidation in a lipid-containing pharmaceutical.
Group IV, claims 42-62, drawn to a method of preventing oxidation using a cosmetic or dermatological composition and a cosmetic or dermatological composition.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical features are apolipoprotein A-IV compounds, which are known in the art, and each claimed method utilizing said compounds requires materially different steps. Specifically, Group I is drawn to treatment of medical conditions [in an animal] that requires consideration of methods of medical treatment related to lipid oxidation resulting in atherosclerosis. Group II is drawn to a method of preventing oxidation in lipid-containing food that requires consideration of lipid biology in plants and animals as well as food handling and storage considerations. Group III is drawn to a method of preventing oxidation in a lipid-containing pharmaceutical that requires consideration of pharmaceutical compositions, formulations and storage. Group IV is drawn to a method for preventing oxidation [of skin] using a cosmetic or dermatological composition and to a cosmetic or dermatological composition which requires consideration of dermatologic or cosmetic compositions as well as methodology of skin treatments that encompass the field of dermatology. Since each method recited above requires different considerations, each method would also encompass wholly different steps to carry out the invention(s). For these reasons, the inventions lack a single inventive concept under PCT Rule 13.1.

(H) MEGLKGQLTP
RANELKATID
QNLEDLRSRL
APLAEGVQEK
LNIHQ;

(I) MEGLAFQ;

(J) MKKNAEELHT
KVSTNIDQLQ
KNLAPLVEDV
QSKLKGNTEG
LQKSLEDLNK
QLDQQVEVFR
RAVEPLGDKFN;

(K) MALVQQ;

(L) MEKFRQQLGS
DSGDVESHLS
FLEKNLREKV
SSF;

(M) MSTLQKKGSP
DQPLALPLPE
QVQEQVQEQV
QPKPLES;

as well as homologues and analogs thereof, wherein:

A =	Ala	= Alanine
R =	Arg	= Arginine
N =	Asn	= Asparagine
D =	Asp	= Aspartic acid
B =	Asx	= Asparagine or aspartic acid
C =	Cys	= Cysteine
Q =	Gln	= Glutamine
E =	Glu	Glutamic acid
Z =	Glx	= Glutamine or Glutamic acid
G	Gly	= Glycine
H =	His	= Histidine
I =	Ile	= Isoleucine
L =	Leu	= Leucine

and expressed as the percentage of protection. Results are means ± S.E. of three measurements. * $p < 0.05$ and ** $p < 0.01$ compared to control.

Fig. 2: **Kinetics of LDL oxidation in the presence of absence of apolipoproteins.** LDL (50 μg/ml) was oxidized using 10 μM $CuSO_4$ at 30°C in a quartz cuvette. Absorbance readings at 234 nm were taken every 5 minutes to measure the formation of conjugated dienes. Conjugated diene formation in LDL was determined in the absence of apolipoproteins (❑), or in the presence of 2.5 μg/ml of apoA-IV (○), 5 μg/ml of apoA-IV (●), rat apoE (△) or human apoE (▲).

Fig. 3: **Inhibitory effect of apoA-IV during the propagation phase of LDL oxidation.** LDL oxidation, monitored by the conjugated diene assay, was allowed to proceed to the propogation phase of oxidation. ApoA-IV was added to the oxidation reaction during the propagation phase, and conjugated dienes were continuously measured in samples containing only LDL (❑), LDL plus tris-saline (×), LDL plus 5 μg/ml of apoA-IV (△), LDL plus 10 μg/ml of apoA-IV (○), and LDL plus 20 μg/ml of apoA-IV (●). The inset shows the change in slope before and after the addition of apoA-IV.

Fig. 4: **ApoA-IV inhibits cell-mediated oxidation of lymph.** Generation of TBARS (nmol/ml of culture medium) by cells incubated in presence or absence of lymph and/or apoA-IV.

CLAIMS

What is claimed is:

1. A method of treating conditions associated with lipid oxidation, comprising: administering a composition comprising a pharmacologically effective amount of an apolipoprotein A-IV compound, wherein the apolipoprotein A-IV compound is a peptide sequence of from 6 to 71 amino acids in length.

2. A method according to claim 1, wherein the peptide has an amino acid sequence selected from the group consisting of:
Met-Phe-Leu-Lys-Ala-Val-Val-Leu-Thr-Val-Ala-Leu-Val-Ala-Ile-Thr-Gly-Thr-Gln-Ala-Glu-Val-Thr-Ser-Asp-Gln-Val-Ala-Asn-Val (SEQ ID NO:1);
Met-Trp-Asp-Tyr-Phe-Thr-Gln-Leu-Ser-Asn-Asn-Ala-Lys-Glu-Ala-Val-Glu-Gln-Leu-Gln-Lys-Thr-Asp-Val-Thr-Gln-Gln-Leu-Asn-Thr-Leu-Phe-Gln-Asp-Lys-Leu-Gly-Asn-Ile-Asn-Thr-Tyr-Ala-Asp-Asp-Leu-Gln-Asn-Lys-Leu-Val-Pro-Phe-Ala-Val-Gln-Leu-Ser-Gly-His-Leu-Thr-Lys-Glu-Thr-Glu-Arg-Val-Arg-Glu-Glu-Ile-Gln-Lys-Glu-Leu-Glu-Asp-Leu-Arg-Ala-Met-Val-Ile (SEQ ID NO:2);
Met-Leu-Pro-His-Ala-Asn-Lys-Val-Ser-Gln (SEQ ID NO:3);
Met-Phe-Gly-Asp-Asn-Val-Gln-Lys-Leu-Gln-Glu-His-Leu-Arg-Pro-Tyr-Ala-Thr-Asp-Leu-Gln-Ala-Gln-Ile-Asn-Ala-Gln-Thr-Gln-Asp (SEQ ID NO:4);
Met-Lys-Arg-Gln-Leu-Thr-Pro-Tyr-Ile-Gln-Arg (SEQ ID NO:5);
Met-Gln-Thr-Thr-Ile-Gln-Asp-Asn-Val-Glu-Asn-Leu-Gln-Ser-Ser (SEQ ID NO:6);
Met-Val-Pro-Phe-Ala-Asn-Glu-Leu-Lys-Glu-Lys-Phe-Asn-Gln-Asn (SEQ ID NO:7);

Met-Glu-Gly-Leu-Lys-Gly-Gln-Leu-Thr-Pro-Arg-Ala-Asn-Glu-Leu-Lys-Ala-Thr-Ile-Asp-Gln-Asn-Leu-Glu-Asp-Leu-Arg-Ser-Arg-Leu-Ala-Pro-Leu-Ala-Glu-Gly-Val-Gln-Glu-Lys-Leu-As n-Ile-His-Gln (SEQ ID NO:8);

Met-Glu-Gly-Leu-Ala-Phe-Gln (SEQ ID NO:9);

Met-Lys-Lys-Asn-Ala-Glu-Glu-Leu-His-Thr-Lys-Val-Ser-Thr-Asn-Ile-Asp-Gln-Leu-Gln-Lys-Asn-Leu-Ala-Pro-Leu-Val-Glu-Asp-Val-Gln-Ser-Lys-Leu-Lys-Gly-Asn-Thr-Glu-Gly-Leu-Gln-Lys-Ser-Leu-Glu-Asp-Leu-Asn-Lys-Gln-Leu-Asp-Gln-Gln-Val-Glu-Val-Phe-Arg-Arg-Ala-Val-Glu-Pro-Leu-Gly-Asp-Lys-Phe-Asn (SEQ ID NO:10);

Met-Ala-Leu-Val-Gln-Gln (SEQ ID NO:11);

Met-Glu-Lys-Phe-Arg-Gln-Gln-Leu-Gly-Ser-Asp-Ser-Gly-Asp-Val-Glu-Ser-His-Leu-Ser-Phe-Leu-Glu-Lys-Asn-Leu-Arg-Glu-Lys-Val-Ser-Ser-Phe (SEQ ID NO:12);

Met-Ser-Thr-Leu-Gln-Lys-Lys-Gly-Ser-Pro-Asp-Gln-Pro-Leu-Ala-Leu-Pro-Leu-Pro-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Pro-Lys-Pro-Leu-Glu-Ser (SEQ ID NO:13);

and derivatives, analogs, homologs, fragments and mixtures thereof.

3. Amethod according to claim 1, wherein the composition further comprises at least one ingredient selected from the group consisting of carriers, fillers, and excipients.

4. A method according to claim 1, wherein the composition further comprises a lipophilic compound.

5. A method according to claim 4, wherein the lipophilic compound is selected from the group consisting of organic solvents, phosphatidyl choline, cholesterol and mixtures thereof.

6. A method according to claim 1, wherein the administering comprises oral administering.

7. A method according to claim 1, wherein the administering comprises parenteral administering.

8. A method according to claim 7, wherein the administering is a dosing method selected from the group consisting of transdermal administering, subcutaneous injecting, intravenous injecting, intraperitoneal injecting, intramuscular injecting, intrasternal injection, intrathecal injection, intraventricular injecting, intracerebroventricular injecting, and infusing.

9. A method according to claim 1, wherein the composition is administered in a unitary dose of from about 1 to about 1000 mg.

10. A method according to claims 9, wherein the unitary dose in administered from about 1 to about 3 time a day.

11. A method of inhibiting the progression of atherosclerosis in a patient in need thereof comprising administering to the patient an effective anti-oxidation amount of a compound of claim 1.

12. A method of treating a patient for atherosclerosis comprising administering to the patient an effective anti-oxidation amount of a compound of claim 2.

13. The method of claim 1, wherein said peptide comprises:

Met-Phe-Leu-Lys-Ala-Val-Val-Leu-Thr-Val-Ala-Leu-Val-Ala-Ile-Thr-Gly-Thr-Gln-Ala-Glu-Val-Thr-Ser-Asp-Gln-Val-Ala-Asn-Val (SEQ ID NO:1).

14. The method of claim 1, wherein said peptide comprises: Met-Trp-Asp-Tyr-Phe-Thr-Gln-Leu-Ser-Asn-Asn-Ala-Lys-Glu-Ala-Val-Glu-Gln-Leu-Gln-Lys-Thr-Asp-Val-Thr-Gln-Gln-Leu-Asn-Thr-Leu-Phe-Gln-Asp-Lys-Leu-Gly-Asn-Ile-Asn-Thr-Tyr-Ala-Asp-Asp-Leu-Gln-Asn-Lys-Leu-Val-Pro-Phe-Ala-Val-Gln-Leu-Ser-Gly-His-Leu-Thr-Lys-Glu-Thr-Glu-Arg-Val-Arg-Glu-Glu-Ile-Gln-Lys-Glu-Leu-Glu-Asp-Leu-Arg-Ala-Met-Val-Ile (SEQ ID NO:2).

15. The method of of claim 1, wherein said peptide comprises: Met-Leu-Pro-His-Ala-Asn-Lys-Val-Ser-Gln (SEQ ID NO:3).

16. The method of claim 1, wherein said peptide comprises: Met-Phe-Gly-Asp-Asn-Val-Gln-Lys-Leu-Gln-Glu-His-Leu-Arg-Pro-Tyr-Ala-Thr-Asp-Leu-Gln-Ala-Gln-Ile-Asn-Ala-Gln-Thr-Gln-Asp (SEQ ID NO:4).

17. The method of claim 1, wherein said peptide comprises: Met-Lys-Arg-Gln-Leu-Thr-Pro-Tyr-Ile-Gln-Arg (SEQ ID NO:5).

18. The method of claim 1, wherein said peptide comprises: Met-Gln-Thr-Thr-Ile-Gln-Asp-Asn-Val-Glu-Asn-Leu-Gln-Ser-Ser (SEQ ID NO:6).

19. The method of claim 1, wherein said peptide comprises: Met-Val-Pro-Phe-Ala-Asn-Glu-Leu-Lys-Glu-Lys-Phe-Asn-Gln-Asn (SEQ ID NO:7).

20. The method of claim 1, wherein said peptide comprises: Met-Glu-Gly-Leu-Lys-Gly-Gln-Leu-Thr-Pro-Arg-Ala-Asn-Glu-Leu-Lys-Ala-Thr-Ile-Asp-Gln-Asn-Leu-Glu-Asp-Leu-Arg-Ser-Arg-Leu-Ala-Pro-Leu-Ala-Glu-Gly-Val-Gln-Glu-Lys-Leu-Asn-Ile-His-Gln (SEQ ID NO:8).

21. The method of claim 1, wherein said peptide comprises: Met-Glu-Gly-Leu-Ala-Phe-Gln (SEQ ID NO:9).

22. The method of claim 1, wherein said peptide comprises: Met-Lys-Lys-Asn-Ala-Glu-Glu-Leu-His-Thr-Lys-Val-Ser-Thr-Asn-Ile-Asp-Gln-Leu-Gln-Lys-Asn-Leu-Ala-Pro-Leu-Val-Glu-Asp-Val-Gln-Ser-Lys-Leu-Lys-Gly-Asn-Thr-Glu-Gly-Leu-Gln-Lys-Ser-Leu-Glu-Asp-Leu-Asn-Lys-Gln-Leu-Asp-Gln-Gln-Val-Glu-Val-Phe-Arg-Arg-Ala-Val-Glu-Pro-Leu-Gly-Asp-Lys-Phe-Asn (SEQ ID NO:10).

23. The method of claim 1, wherein said peptide comprises: Met-Ala-Leu-Val-Gln-Gln (SEQ ID NO:11).

24. The method of claim 1, wherein said peptide comprises: Met-Glu-Lys-Phe-Arg-Gln-Gln-Leu-Gly-Ser-Asp-Ser-Gly-Asp-Val-Glu-Ser-His-Leu-Ser-Phe-Leu-Glu-Lys-Asn-Leu-Arg-Glu-Lys-Val-Ser-Ser-Phe (SEQ ID NO:12).

25. The method of claim 1, wherein said peptide comprises: Met-Ser-Thr-Leu-Gln-Lys-Lys-Gly-Ser-Pro-Asp-Gln-Pro-Leu-Ala-Leu-Pro-Leu-Pro-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Pro-Lys-Pro-Leu-Glu-Ser (SEQ ID NO:13).

26. A method of preventing oxidation in a lipid-containing food comprising incorporating in the food an oxidation-inhibiting amount of an apolipoprotein (apo) A-IV compound to protect the food from oxidation.

27. A method according to claim 26, wherein the apolipoprotein (apo) A-IV compound is selected from the group consisting of apolipoprotein (apo) A-IV, derivatives, analogs, homologs, fragments and mixtures thereof.

28. A method according to claim 27, wherein the apolipoprotein (apo) A-IV molecule is a peptide sequence from about 5 to about 90 amino acids in length.

29. A method according to claim 28, wherein the peptide has an amino acid sequence selected from the group consisting of:

Met-Phe-Leu-Lys-Ala-Val-Val-Leu-Thr-Val-Ala-Leu-Val-Ala-Ile-Thr-Gly-Thr-Gln-Ala-Glu-Val-Thr-Ser-Asp-Gln-Val-Ala-Asn-Val (SEQ ID NO:1);

Met-Trp-Asp-Tyr-Phe-Thr-Gln-Leu-Ser-Asn-Asn-Ala-Lys-Glu-Ala-Val-Glu-Gln-Leu-Gln-Lys-Thr-Asp-Val-Thr-Gln-Gln-Leu-Asn-Thr-Leu-Phe-Gln-Asp-Lys-Leu-Gly-Asn-Ile-Asn-Thr-Tyr-Ala-Asp-Asp-Leu-Gln-Asn-Lys-Leu-Val-Pro-Phe-Ala-Val-Gln-Leu-Ser-Gly-His-Leu-Thr-Lys-Glu-Thr-Glu-Arg-Val-Arg-Glu-Glu-Ile-Gln-Lys-Glu-Leu-Glu-Asp-Leu-Arg-Ala-Met-Val-Ile (SEQ ID NO:2);

Met-Leu-Pro-His-Ala-Asn-Lys-Val-Ser-Gln (SEQ ID NO:3);

Met-Phe-Gly-Asp-Asn-Val-Gln-Lys-Leu-Gln-Glu-His-Leu-Arg-Pro-Tyr-Ala-Thr-Asp-Leu-Gln-Ala-Gln-Ile-Asn-Ala-Gln-Thr-Gln-Asp (SEQ ID NO:4);

Met-Lys-Arg-Gln-Leu-Thr-Pro-Tyr-Ile-Gln-Arg (SEQ ID NO:5);

Met-Gln-Thr-Thr-Ile-Gln-Asp-Asn-Val-Glu-Asn-Leu-Gln-Ser-Ser (SEQ ID NO:6);

Met-Val-Pro-Phe-Ala-Asn-Glu-Leu-Lys-Glu-Lys-Phe-Asn-Gln-Asn (SEQ ID NO:7);

Met-Glu-Gly-Leu-Lys-Gly-Gln-Leu-Thr-Pro-Arg-Ala-Asn-Glu-Leu-Lys-Ala-Thr-Ile-Asp-Gln-Asn-Leu-Glu-Asp-Leu-Arg-Ser-Arg-Leu-Ala-Pro-Leu-Ala-Glu-Gly-Val-Gln-Glu-Lys-Leu-Asn-Ile-His-Gln (SEQ ID NO:8);

Met-Glu-Gly-Leu-Ala-Phe-Gln (SEQ ID NO:9);

Met-Lys-Lys-Asn-Ala-Glu-Glu-Leu-His-Thr-Lys-Val-Ser-Thr-Asn-Ile-Asp-Gln-Leu-Gln-Lys-Asn-Leu-Ala-Pro-Leu-Val-Glu-Asp-Val-Gln-Ser-Lys-Leu-Lys-Gly-Asn-Thr-Glu-Gly-Leu-Gln-Lys-Ser-Leu-Glu-Asp-Leu-Asn-Lys-Gln-Leu-Asp-Gln-Gln-Val-Glu-Val-Phe-Arg-Arg-Ala-Val-Glu-Pro-Leu-Gly-Asp-Lys-Phe-Asn (SEQ ID NO:10);

Met-Ala-Leu-Val-Gln-Gln (SEQ ID NO:11);

Met-Glu-Lys-Phe-Arg-Gln-Gln-Leu-Gly-Ser-Asp-Ser-Gly-Asp-Val-Glu-Ser-His-Leu-Ser-Phe-Leu-Glu-Lys-Asn-Leu-Arg-Glu-Lys-Val-Ser-Ser-Phe (SEQ ID NO:12);

Met-Ser-Thr-Leu-Gln-Lys-Lys-Gly-Ser-Pro-Asp-Gln-Pro-Leu-Ala-Leu-Pro-Leu-Pro-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Pro-Lys-Pro-Leu-Glu-Ser (SEQ ID NO:13);

and derivatives, analogs, homologs, fragments and mixtures thereof.

30. A method according to claim 27, wherein the composition further comprises at least one ingredient selected from the group consisting of carriers, fillers, and excipients.

31. A method according to claim 27, wherein the apolipoprotein A-IV compound makes up about 0.01% to about 10% of the final weight of the food product.

32. A method according to claim 26, wherein the apolipoprotein A-IV compound makes up about 0.02% to about 5% of the final weight of the food product.

33. A method of preventing oxidation in a lipid-containing pharmaceutical comprising incorporating in the pharmaceutical an oxidation-inhibiting amount of an apolipoprotein (apo) A-IV compound to protect the pharmaceutical from oxidation.

34. A method according to claim 33, wherein the apolipoprotein (apo) A-IV compound is selected from the group consisting of apolipoprotein (apo) A-IV, derivatives, analogs, homologs, fragments and mixtures thereof.

35. A method according to claim 34, wherein the apolipoprotein (apo) A-IV molecule is a peptide sequence from about 5 to about 90 amino acids in length.

36. A method according to claim 34, wherein the peptide has an amino acid sequence selected from the group consisting of:
Met-Phe-Leu-Lys-Ala-Val-Val-Leu-Thr-Val-Ala-Leu-Val-Ala-Ile-Thr-Gly-Thr-Gln-Ala-Glu-Val-Thr-Ser-Asp-Gln-Val-Ala-Asn-Val (SEQ ID NO:1);

Met-Trp-Asp-Tyr-Phe-Thr-Gln-Leu-Ser-Asn-Asn-Ala-Lys-Glu-Ala-Val-Glu-Gln-Leu-Gln-Lys-Thr-Asp-Val-Thr-Gln-Gln-Leu-Asn-Thr-Leu-Phe-Gln-Asp-Lys-Leu-Gly-Asn-Ile-Asn-Thr-Tyr-Ala-Asp-Asp-Leu-Gln-Asn-Lys-Leu-Val-Pro-Phe-Ala-Val-Gln-Leu-Ser-Gly-His-Leu-Thr-Lys-Glu-Thr-Glu-Arg-Val-Arg-Glu-Glu-Ile-Gln-Lys-Glu-Leu-Glu-Asp-Leu-Arg-Ala-Met-Val-Ile (SEQ ID NO:2);
Met-Leu-Pro-His-Ala-Asn-Lys-Val-Ser-Gln (SEQ ID NO:3);
Met-Phe-Gly-Asp-Asn-Val-Gln-Lys-Leu-Gln-Glu-His-Leu-Arg-Pro-Tyr-Ala-Thr-Asp-Leu-Gln-Ala-Gln-Ile-Asn-Ala-Gln-Thr-Gln-Asp (SEQ ID NO:4);
Met-Lys-Arg-Gln-Leu-Thr-Pro-Tyr-Ile-Gln-Arg (SEQ ID NO:5);
Met-Gln-Thr-Thr-Ile-Gln-Asp-Asn-Val-Glu-Asn-Leu-Gln-Ser-Ser (SEQ ID NO:6);

Met-Val-Pro-Phe-Ala-Asn-Glu-Leu-Lys-Glu-Lys-Phe-Asn-Gln-Asn (SEQ ID NO:7);
Met-Glu-Gly-Leu-Lys-Gly-Gln-Leu-Thr-Pro-Arg-Ala-Asn-Glu-Leu-Lys-Ala-Thr-Ile-Asp-Gln-Asn-Leu-Glu-Asp-Leu-Arg-Ser-Arg-Leu-Ala-Pro-Leu-Ala-Glu-Gly-Val-Gln-Glu-Lys-Leu-Asn-Ile-His-Gln (SEQ ID NO:8);
Met-Glu-Gly-Leu-Ala-Phe-Gln (SEQ ID NO:9);
Met-Lys-Lys-Asn-Ala-Glu-Glu-Leu-His-Thr-Lys-Val-Ser-Thr-Asn-Ile-Asp-Gln-Leu-Gln-Lys-Asn-Leu-Ala-Pro-Leu-Val-Glu-Asp-Val-Gln-Ser-Lys-Leu-Lys-Gly-Asn-Thr-Glu-Gly-Leu-Gln-Lys-Ser-Leu-Glu-Asp-Leu-Asn-Lys-Gln-Leu-Asp-Gln-Gln-Val-Glu-Val-Phe-Arg-Arg-Ala-Val-Glu-Pro-Leu-Gly-Asp-Lys-Phe-Asn (SEQ ID NO:10);
Met-Ala-Leu-Val-Gln-Gln (SEQ ID NO:11);
Met-Glu-Lys-Phe-Arg-Gln-Gln-Leu-Gly-Ser-Asp-Ser-Gly-Asp-Val-Glu-Ser-His-Leu-Ser-Phe-Leu-Glu-Lys-Asn-Leu-Arg-Glu-Lys-Val-Ser-Ser-Phe (SEQ ID NO:12);
Met-Ser-Thr-Leu-Gln-Lys-Lys-Gly-Ser-Pro-Asp-Gln-Pro-Leu-Ala-Leu-Pro-Leu-Pro-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Pro-Lys-Pro-Leu-Glu-Ser (SEQ ID NO:13);
and derivatives, analogs, homologs, fragments and mixtures thereof.

37. A method according to claim 36, wherein the composition further comprises at least one ingredient selected from the group consisting of carriers, fillers, and excipients.

38. A method according to claim 36, wherein the Apolipoprotein A-IV compound makes up about 0.01 to about 25% of the final weight of the pharmaceutical product.

39. A method according to claim 36, wherein the apolipoprotein A-IV compound makes up about 0.05% to about 10% of the final weight of the pharmaceutical

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product.

40. A method of preventing oxidation using a cosmetic or dermatological composition comprising incorporating, in a suitable vehicle containing cosmetic or dermatological composition, an oxidation-inhibiting amount of an apolipoprotein (apo) A-IV compound to protect the containing cosmetic or dermatological composition from oxidation.

41. A method according to claim 40, wherein the apolipoprotein (apo) A-IV compound is selected from the group consisting of apolipoprotein (apo) A-IV, derivatives, analogs, homologs, fragments and mixtures thereof.

42. A method according to claim 41, wherein the apolipoprotein (apo) A-IV molecule is a peptide sequence from about 5 to about 90 amino acids in length.

43. A method according to claim 42, wherein the peptide has an amino acid sequence selected from the group consisting of:
Met-Phe-Leu-Lys-Ala-Val-Val-Leu-Thr-Val-Ala-Leu-Val-Ala-Ile-Thr-Gly-Thr-Gln-Ala-Glu-Val-Thr-Ser-Asp-Gln-Val-Ala-Asn-Val (SEQ ID NO:1);
Met-Trp-Asp-Tyr-Phe-Thr-Gln-Leu-Ser-Asn-Asn-Ala-Lys-Glu-Ala-Val-Glu-Gln-Leu-Gln-Lys-Thr-Asp-Val-Thr-Gln-Gln-Leu-Asn-Thr-Leu-Phe-Gln-Asp-Lys-Leu-Gly-Asn-Ile-Asn-Thr-Tyr-Ala-Asp-Asp-Leu-Gln-Asn-Lys-Leu-Val-Pro-Phe-Ala-Val-Gln-Leu-Ser-Gly-His-Leu-Thr-Lys-Glu-Thr-Glu-Arg-Val-Arg-Glu-Glu-Ile-Gln-Lys-Glu-Leu-Glu-Asp-Leu-Arg-Ala-Met-Val-Ile (SEQ ID NO:2);
Met-Leu-Pro-His-Ala-Asn-Lys-Val-Ser-Gln (SEQ ID NO:3);
Met-Phe-Gly-Asp-Asn-Val-Gln-Lys-Leu-Gln-Glu-His-Leu-Arg-Pro-Tyr-Ala-Thr-

Asp-Leu-Gln-Ala-Gln-Ile-Asn-Ala-Gln-Thr-Gln-Asp (SEQ ID NO:4);
Met-Lys-Arg-Gln-Leu-Thr-Pro-Tyr-Ile-Gln-Arg (SEQ ID NO:5);
Met-Gln-Thr-Thr-Ile-Gln-Asp-Asn-Val-Glu-Asn-Leu-Gln-Ser-Ser (SEQ ID NO:6);
Met-Val-Pro-Phe-Ala-Asn-Glu-Leu-Lys-Glu-Lys-Phe-Asn-Gln-Asn (SEQ ID NO:7);
Met-Glu-Gly-Leu-Lys-Gly-Gln-Leu-Thr-Pro-Arg-Ala-Asn-Glu-Leu-Lys-Ala-Thr-Ile-Asp-Gln-Asn-Leu-Glu-Asp-Leu-Arg-Ser-Arg-Leu-Ala-Pro-Leu-Ala-Glu-Gly-Val-Gln-Glu-Lys-Leu-Asn-Ile-His-Gln (SEQ ID NO:8);
Met-Glu-Gly-Leu-Ala-Phe-Gln (SEQ ID NO:9);
Met-Lys-Lys-Asn-Ala-Glu-Glu-Leu-His-Thr-Lys-Val-Ser-Thr-Asn-Ile-Asp-Gln-Leu-Gln-Lys-Asn-Leu-Ala-Pro-Leu-Val-Glu-Asp-Val-Gln-Ser-Lys-Leu-Lys-Gly-Asn-Thr-Glu-Gly-Leu-Gln-Lys-Ser-Leu-Glu-Asp-Leu-Asn-Lys-Gln-Leu-Asp-Gln-Gln-Val-Glu-Val-Phe-Arg-Arg-Ala-Val-Glu-Pro-Leu-Gly-Asp-Lys-Phe-Asn (SEQ ID NO:10);
Met-Ala-Leu-Val-Gln-Gln (SEQ ID NO:11);
Met-Glu-Lys-Phe-Arg-Gln-Gln-Leu-Gly-Ser-Asp-Ser-Gly-Asp-Val-Glu-Ser-His-Leu-Ser-Phe-Leu-Glu-Lys-Asn-Leu-Arg-Glu-Lys-Val-Ser-Ser-Phe (SEQ ID NO:12);
Met-Ser-Thr-Leu-Gln-Lys-Lys-Gly-Ser-Pro-Asp-Gln-Pro-Leu-Ala-Leu-Pro-Leu-Pro-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Pro-Lys-Pro-Leu-Glu-Ser (SEQ ID NO:13);
and derivatives, analogs, homologs, fragments and mixtures thereof.

44. A method according to claim 43, wherein the composition further comprises at least one ingredient selected from the group consisting of carriers, fillers, and excipients.

45. A method according to claim 43, wherein the apolipoprotein (apo) A-IV

compound is present at a concentration between about 0.005% and about 25% by weight with respect to the total weight of the composition.

46. A method according to claim 43, wherein the apolipoprotein (apo) A-IV compound is present at a concentration between about 0.05% and about 10% by weight with respect to the total weight of the composition.

47. A cosmetic or dermatological composition containing, in a suitable vehicle, an oxidation-inhibiting amount of an apolipoprotein (apo) A-IV compound.

48. A composition according to claim 47, wherein the apolipoprotein (apo) A-IV compound is selected from the group consisting of apolipoprotein (apo) A-IV, derivatives, analogs, homologs, fragments and mixtures thereof.

49. A composition according to claim 48, wherein the apolipoprotein (apo) A-IV molecule is a peptide sequence from about 5 to about 90 amino acids in length.

50. A composition according to claim 49, wherein the peptide has an amino acid sequence selected from the group consisting of:
Met-Phe-Leu-Lys-Ala-Val-Val-Leu-Thr-Val-Ala-Leu-Val-Ala-Ile-Thr-Gly-Thr-Gln-Ala-Glu-Val-Thr-Ser-Asp-Gln-Val-Ala-Asn-Val (SEQ ID NO:1);
Met-Trp-Asp-Tyr-Phe-Thr-Gln-Leu-Ser-Asn-Asn-Ala-Lys-Glu-Ala-Val-Glu-Gln-Leu-Gln-Lys-Thr-Asp-Val-Thr-Gln-Gln-Leu-Asn-Thr-Leu-Phe-Gln-Asp-Lys-Leu-Gly-Asn-Ile-Asn-Thr-Tyr-Ala-Asp-Asp-Leu-Gln-Asn-Lys-Leu-Val-Pro-Phe-Ala-Val-Gln-Leu-Ser-Gly-His-Leu-Thr-Lys-Glu-Thr-Glu-Arg-Val-Arg-Glu-Glu-Ile-Gln-Lys-Glu-Leu-Glu-Asp-Leu-Arg-Ala-Met-Val-Ile (SEQ ID NO:2);

Met-Leu-Pro-His-Ala-Asn-Lys-Val-Ser-Gln (SEQ ID NO:3);
Met-Phe-Gly-Asp-Asn-Val-Gln-Lys-Leu-Gln-Glu-His-Leu-Arg-Pro-Tyr-Ala-Thr-Asp-Leu-Gln-Ala-Gln-Ile-Asn-Ala-Gln-Thr-Gln-Asp (SEQ ID NO:4);
Met-Lys-Arg-Gln-Leu-Thr-Pro-Tyr-Ile-Gln-Arg (SEQ ID NO:5);
Met-Gln-Thr-Thr-Ile-Gln-Asp-Asn-Val-Glu-Asn-Leu-Gln-Ser-Ser (SEQ ID NO:6);
Met-Val-Pro-Phe-Ala-Asn-Glu-Leu-Lys-Glu-Lys-Phe-Asn-Gln-Asn (SEQ ID NO:7);
Met-Glu-Gly-Leu-Lys-Gly-Gln-Leu-Thr-Pro-Arg-Ala-Asn-Glu-Leu-Lys-Ala-Thr-Ile-Asp-Gln-Asn-Leu-Glu-Asp-Leu-Arg-Ser-Arg-Leu-Ala-Pro-Leu-Ala-Glu-Gly-Val-Gln-Glu-Lys-Leu-Asn-Ile-His-Gln (SEQ ID NO:8);
Met-Glu-Gly-Leu-Ala-Phe-Gln (SEQ ID NO:9);
Met-Lys-Lys-Asn-Ala-Glu-Glu-Leu-His-Thr-Lys-Val-Ser-Thr-Asn-Ile-Asp-Gln-Leu-Gln-Lys-Asn-Leu-Ala-Pro-Leu-Val-Glu-Asp-Val-Gln-Ser-Lys-Leu-Lys-Gly-Asn-Thr-Glu-Gly-Leu-Gln-Lys-Ser-Leu-Glu-Asp-Leu-Asn-Lys-Gln-Leu-Asp-Gln-Gln-Val-Glu-Val-Phe-Arg-Arg-Ala-Val-Glu-Pro-Leu-Gly-Asp-Lys-Phe-Asn (SEQ ID NO:10);
Met-Ala-Leu-Val-Gln-Gln (SEQ ID NO:11);
Met-Glu-Lys-Phe-Arg-Gln-Gln-Leu-Gly-Ser-Asp-Ser-Gly-Asp-Val-Glu-Ser-His-Leu-Ser-Phe-Leu-Glu-Lys-Asn-Leu-Arg-Glu-Lys-Val-Ser-Ser-Phe (SEQ ID NO:12);
Met-Ser-Thr-Leu-Gln-Lys-Lys-Gly-Ser-Pro-Asp-Gln-Pro-Leu-Ala-Leu-Pro-Leu-Pro-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Glu-Gln-Val-Gln-Pro-Lys-Pro-Leu-Glu-Ser (SEQ ID NO:13);
and derivatives, analogs, homologs, fragments and mixtures thereof.

51. The cosmetic or dermatological composition of claim 50, wherein the composition is in the form of a suspension or dispersion in a solvent or a fatty substance, or in the form of an emulsion, or in the form of an ointment, a gel, a solid

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stick or an aerosol foam.

52 The cosmetic or dermatological composition of claim 50, in a form wherein the cosmetically acceptable carrier is selected from the group consisting of a lotion, a gel, a cream, a milk, a powder, a solid stick, a foam and a spray.

53. The cosmetic or dermatological composition according to claim 50, wherein the composition additionally contains cosmetic adjuvants selected from the group consisting of lower alcohols, polyols, esters of fatty acids, oils, and waxes, solvents, silicones, thickeners, emollients, UV-A sunscreens, UV-B sunscreens, broad band sunscreens, antifoam agents, hydrating agents, perfumes, stabilizers, surfactants, fillers, sequestrants, anionic, cationic, nonionic and amphoteric polymers and mixtures thereof, propellants, alkalifying and acidifying agents, dyes and metal oxide pigments.

54. The composition according to claim 50, wherein the apolipoprotein A-IV compound is present at a concentration between about 0.005% and about 15% by weight with respect to the total weight of the composition.

55. The cosmetic or dermatological composition of claim 50, which further contains either at least one basic agent or includes at least one tocopherol or a derivative.

56. The cosmetic or dermatological composition of claim 55, wherein the composition contains from about 0.5 to about 20 weight percent of a tocopherol or derivative thereof, about 0.5 to about 50 weight percent of a basic agent and about 0.5

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to about 90 weight percent of the apolipoprotein A-IV compound.

57. The cosmetic or dermatological composition of claim 56, wherein the basic agent is selected from the group consisting of sodium hydroxide, triethanolamine, a basic amino acid, such as lysine or arginine and mixtures thereof.

58. The cosmetic or dermatological composition of claim 55, wherein the composition contains from about 0.05 to about 2.0 weight percent of a tocopherol or derivative thereof, about 0.05 to about 5.0 weight percent of a basic agent and about 0.05 to about 9.0 weight percent of the apolipoprotein A-IV compound.

59. The cosmetic or dermatological composition of claim 55, wherein the composition additionally contains one or more compounds selected from the group consisting of wetting agents; depigmenting agents such as hydroquinone, azelaic acid, caffeic acid or kojic acid; emollients; moisturizing agents such as glycerol, PEG 400, thiamorpholinone and its derivatives or alternatively urea; antiseborrhoeic or antiacne agents such as S-carboxymethylcysteine, S-benzylcysteamine, salts or derivatives thereof, benzoyl peroxide; antibiotics such as erythromycin and esters thereof, neomycin, clindamycin and esters thereof, tetracyclines; antifungal agents such as ketoconazole or 4,5-polymethylene-3-isothiazolidones; agents promoting hair regrowth, such as Minoxidil (2,4-diamino-6-piperidinopyrimidine 3-oxide) and derivatives thereof, Diazoxide (7-chloro-3-methyl-1,2,4-benzothiadiazine-1,1-dioxide) and Phenytoin (5,4-diphenyl-2,4-imidazolidinedione); non-steroidal anti-inflammatory agents; carotenoids and especially beta -carotene; anti-psoriatic agents such as anthralin and derivatives thereof; 5,8,11,14-eicosatetraynoic and 5,8,11-eicosatrynoic acids and esters and amides thereof; taste- or flavor-enhancing agents;

preservatives such as parahydroxybenzoic acid esters; stabilizing agents; moisture regulating agents; pH regulating agents; osmotic pressure modifying agents; emulsifying agents; UV-A and UV-B screening agents; and other antioxidants such as alpha -tocopherol, butylated hydroxyanisole or butylated hydroxytoluene.

60. Cosmetic composition according to claim 59, wherein the composition additionally contains cosmetic adjuvants selected from the group consisting of lower alcohols, polyols, esters of fatty acids, oils, waxes, solvents, silicones, thickeners, emollients, UV-A sunscreens, UV-B sunscreens, broad band sunscreens, antifoam agents, hydrating agents, perfumes, stabilizers, surfactants, fillers, sequestrants, anionic, cationic, nonionic and amphoteric polymers and mixtures thereof, propellants, alkalifying and acidifying agents, dyes and metal oxide pigments.

61. The cosmetic or dermatological composition of claim 50, further comprising an ingredient selected from the group consisting of wetting agents; depigmenting; emollients; moisturizing agents; antiseborrhoeic agents; antiacne agents; antibiotics; antifungal agents; agents promoting hair regrowth; non-steroidal anti-inflammatory agents; antioxidants; anti-psoriatic agents; 5,8,11,14-eicosatetraynoic acid and esters and amides thereof; 5,8,11-eicosatrynoic acid and esters and amides thereof; taste-flavor-enhancing agents; flavor-enhancing agents; preservatives; pH regulating agents; osmotic pressure modifying agents; emulsifying agents; UV-A and UV-B screening agents; and mixture thereof.

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